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10/574,730	01/05/2007	Robert A. Burne	5853-454-1	5558

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EXAMINER	
TONGUE, LAKIA J	
ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
11/25/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/574,730	BURNE ET AL.	
	Examiner	Art Unit	
	LAKIA J. TONGUE	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21-27 and 34-59* is/are pending in the application.

4a) Of the above claim(s) *14-17,24-27 and 53-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-12,18,19,21-23,34-38 and 44-52* is/are rejected.

7)☒ Claim(s) *9,13 and 39-43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Claims 1-19, 21-27 and 34-59 are pending. Claims 14-17, 24-27 and 53-59 were previously withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 20 and 28-33 have been canceled. Claims 1, 3, 4, 8, 18, 34 and 57 have been amended. Claims 1-13, 18, 19, 21-23, 34-52 are currently under examination.

Objections Withdrawn

2. In view of Applicant's amendment to the specification, the objection to the disclosure because it contains an embedded hyperlink and/or other form of browser-executable code (see pages 20, 24 and 56) is withdrawn.

Rejections Withdrawn

3. In view of the cancellation of claims 28-33, the rejection of claims 28-33 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn.

4. In view of Applicant's argument, the rejection of claims 1-5 under 35 U.S.C. 102(b) as being anticipated by Chen et al. (Infection and Immunity, 1996; 64(2): 585-592) is withdrawn.

Objections Maintained

5. The objection to claims 9, 13 and 39-43 for depending on a rejected based claim is maintained for the reasons set forth in the previous office action.

Rejections Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The rejection of claims 1-5, 7, 8, 10, 12, 18, 19, 23, 34-38 and 44-52 under 35 U.S.C. 102(b) as being anticipated by Clancy et al. (Infection and Immunity, 2000; 68(5): 2621-2629) is maintained for the reasons set forth in the previous office action.

Applicant argues that:

1) Clancy et al. disclose urease-expressing bacteria, nonureolytic *S. mutans*, which lacks the ability to express a nickel transporter.

Applicant's arguments have been considered but are deemed non-persuasive.

The rejected claims are drawn to a recombinant bacterial cell comprising an isolated nucleic acid construct, said cell expressing at least one alkalinizing enzyme and a nickel transporter.

With regard to Point 1, while the urease expressing bacteria of Clancy et al. do not specifically disclose that it expresses a nickel transporter; Clancy et al. do disclose that recombinant, ureolytic strains of Streptococcus mutans were constructed. Specifically, the ureABCEFGD operon from Streptococcus salivarius 57.I was integrated into the S. mutans chromosome. Applicant's disclosure teaches that a recombinant cell which includes a nickel transporter is a recombinant *S. mutans*, which express *ure*ABCEFGD (see page 22, lines 4-5). Absent evidence to the contrary, the recombinant bacterial cell of Clancy et al. necessarily expresses a nickel transporter.

As previously presented, Clancy et al. disclose the use of urease enzymes of oral bacteria to hydrolyze urea to ammonia, which can neutralize plaque acids. Clancy et al. disclose that recombinant, ureolytic strains of Streptococcus mutans were constructed. Specifically, the ureABCEFGD operon from Streptococcus salivarius 57.I was integrated into the S. mutans chromosome in such a way that the operon was transcribed from a weak, cognate promoter in S. mutans ACUS4 or a stronger promoter in S. mutans ACUS6. Clancy et al. disclose that both strains expressed $NiCl_2$-dependent urease activity. Moreover, Clancy et al. disclose that the integration of the antibiotic resistance and urease genes into the *S. mutans* chromosome was confirmed by Southern blotting (see page 2622-DNA manipulations). Clancy et al. disclose that the urease genes were cloned as a cassette into the *S. mutans* lac sequences on the integration vector with concomitant replacement of the tetracycline resistance gene (see page 2622). Clancy et al. disclose that recombinant strains confirmed that integration of the *ure* genes and selective markers occurred in the *lac* locus (see page 2623). Clancy et al. disclose that when no additional $NiCl_2$ was added to the medium the strains expressed urease (see page 2624). Clancy et al. disclose that recombinant strains produce functional urease in the absence of exogenous nickel *in vitro* and *in vivo* (see page 2627-discussion). Clancy et al. disclose that the use of alkali-generating bacteria should be considered for replacement therapy (see page 2628). Clancy et al. disclose that subjects were infected with the recombinant strain and fed a cariogenic diet with drinking water containing 25 mM urea and 50 μM $NiCl_2$ had relatively high levels of oral urease activity, as well as dramatic decreases in the prevalence of smooth-surface caries and the severity of sulcal caries, relative to controls, indicating that ureolytic bacteria may be useful to promote dental health (see abstract).

The instantly claimed invention is identical to that of the prior art. Absent evidence to the contrary, the recombinant bacteria of Clancy et al. necessarily produces an agmatine deiminase enzyme, the vector is necessarily stably integrated into the

genome, the vector necessarily targets a *mtl* gene and the *ure*ABCEFGD necessarily comprises a nickel transporter.

Since the Office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

7. The rejection of claims 1-6, 10, 11, 18, 19, 21, 38 and 52 under 35 U.S.C. 102(a) as being anticipated by Dong et al. (Applied and Environmental Microbiology, 2002; 68(11): 5549-5553) is maintained for the reasons set forth in the previous office action.

Applicant argues that:

1) Dong discloses an arginine deminanse system incapable of expressing nickel transporter genes.

Applicant's arguments have been considered but are deemed non-persuasive.

The rejected claims are drawn to a recombinant bacterial cell comprising an isolated nucleic acid construct, said cell expressing at least one alkalinizing enzyme and a nickel transporter.

With regard to Point 1, while the urease expressing bacteria of Dong does not specifically disclose that it expresses a nickel transporter; Dong discloses that the genes encoding enzymes for arginine catabolism are identified and were genetically engineered to express urease genes of *S. mutans* (see page 5552; Functional analysis of ArcR). Applicant's disclosure teaches that a recombinant cell which includes a nickel transporter is a recombinant *S. mutans*, which express *ure*ABCEFGD (see page 22, lines 4-5). Absent evidence to the contrary, the recombinant bacterial cell of Dong necessarily expresses a nickel transporter.

As previously presented, Dong et al. disclose that an arginine deiminase (AD) system (ADS) is one of two major ammonia-generating pathways in the oral cavity that play important roles in oral biofilm pH homeostasis and oral biofilm ecology. Dong et al. disclose that *Streptococcus gordonii* ADS and the ADS gene cluster were isolated from subgenomic DNA libraries of *S. gordonii* DL1 by using an *arcB*-specific probe (see abstract). Dong et al. disclose genes encoding enzymes for arginine in *S. gordonii.* Dong et al. disclose genetically engineered, ammonia-producing oral streptococci as potential agents for the control of dental caries expressing the urease genes of *Streptococcus salivarius* in *Streptococcus mutans* (see page 5552). Dong et al. disclose the similarities between the deduced amino acids sequences of *arc*ABCDTR of *S. gordonii* (see page 5551). Moreover, Dong et al. disclose that conserved amino acid residues for arginine binding were found in *S. gordonii* (see page 5551).

The instantly claimed invention is identical to that of the prior art. Absent evidence to the contrary, the vector of Dong et al. necessarily targets a *mtl* gene.

Since the Office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The rejection of claim 23 under 35 U.S.C. 103(a) as being unpatentable over Dong et al. (Applied and Environmental Microbiology, 2002; 68(11): 5549-5553) as applied to claims 1-6, 10, 11, 18, 19, 21 and 52 above is maintained for the reasons set forth in the previous office action.

Applicant argues that:

1) Dong's arginine deminanse system lacks nickel transporter genes; therefore, Dong fails to teach all limitations of claim 23.

Applicant's arguments have been considered but are deemed non-persuasive.

The rejected claims are drawn to a recombinant bacterial cell comprising an isolated nucleic acid construct, said cell expressing at least one alkalinizing enzyme and a nickel transporter.

With regard to Point 1, contrary to Applicant's assertion, while the urease expressing bacteria of Dong does not specifically disclose that it expresses a nickel transporter; Dong discloses that the genes encoding enzymes for arginine catabolism are identified and were genetically engineered to express urease genes of *S. mutans* (see page 5552; Functional analysis of ArcR). Applicant's disclosure teaches that a recombinant cell which includes a nickel transporter is a recombinant *S. mutans*, which express *ure*ABCEFGD (see page 22, lines 4-5). Absent evidence to the contrary, the recombinant bacterial cell of Dong necessarily expresses a nickel transporter and therefore meets the limitation of claim 23.

As previously presented, Dong et al. disclose that an arginine deiminase (AD) system (ADS) is one of two major ammonia-generating pathways in the oral cavity that play important roles in oral biofilm pH homeostasis and oral biofilm ecology. Dong et al. disclose that *Streptococcus gordonii* ADS and the ADS gene cluster were isolated from subgenomic DNA libraries of *S. gordonii* DL1 by using an *arcB*-specific probe (see abstract). Dong et al. disclose genes encoding enzymes for arginine in *S. gordonii.* Dong et al. disclose genetically engineered, ammonia-producing oral streptococci as potential agents for the control of dental caries expressing the urease genes of *Streptococcus salivarius* in *Streptococcus mutans* (see page 5552). Dong et al. disclose the similarities between the deduced amino acids sequences of *arc*ABCDTR of *S. gordonii* (see page 5551). Moreover, Dong et al. disclose that conserved amino acid residues for arginine binding were found in *S. gordonii* (see page 5551).

Dong et al. do not specifically disclose that the carrier is selected from the group consisting of a chewing gum, toothpaste, a lozenge, a powder, a gel, an ointment, a cream, a liquid, a mouthwash, a rinse and a candy.

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Dong et al. to include said recombinant bacterial cell with a carrier selected from the group consisting of a chewing gum, toothpaste, a lozenge, a powder, a gel, an ointment, a cream, a liquid, a mouthwash, a rinse and a candy because Dong et al. disclose that the study provides the foundation for exploiting the use of arginine catabolism to moderate plaque acidification and to control the emergence of a cariogenic flora see pages 5552-3) and Clancy disclose that ureolytic bacteria maybe useful to promote dental health (see abstract). Moreover, the claim would have been obvious because the design incentives or market forces provided a reason to make an adaptation, and the invention resulted from application of the prior knowledge in a predictable manner (see the recent Board decision *Ex parte Smith,-- USPQ2d--,* slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR, 82 USPQ2d* at 1396). One would have had a reasonable expectation, barring evidence to the contrary, that the composition would be effective.

Conclusion

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKIA J. TONGUE whose telephone number is (571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LJT
11/19/09

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645